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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,324	01/04/2002	H. William Bosch	029318-0107	2223

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EXAMINER	
HAGHIGHATIAN, MINA	
ART UNIT	**PAPER NUMBER**
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/035,324	BOSCH ET AL.	
	Examiner	Art Unit	
	Mina Haghighatian	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/30/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-11 and 13-34* is/are pending in the application.

4a) Of the above claim(s) *15-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-11,13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/31/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/07 has been entered.

Receipt is acknowledged of the Amendments and Remarks filed on 11/30/07 and an IDS filed on 10/31/07. No claims have been amended, cancelled or newly added. Claims 15-34 remain withdrawn. Accordingly, claims **1-7, 9-11 and 13-14** remain under examination.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-7, 9-11 and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wiedmann et al (5,747,001) in view of Desai et al (US 20070117862).

Wiedmann et al teach aerosols containing droplets of an aqueous **dispersion** of nanoparticles of insoluble **beclomethasone** particles having a surface modifier on the

surface thereof. Representative examples of surface modifiers include gelatin, benzalkonium chloride, PVA, sorbitans, etc (see col. 3, line 30 to col. 4, line 45). A suitable surfactant is **tyloxapol** (see col. 4, lines 49-60), the particles are preferably less than 400 nm in size, or more preferably less than 250 and most preferably **less than 100 nm** in size (see col. 6, lines 8-15 and col. 10, lines 25-35). The process of making such nanoparticles includes attrition and **filtration** (see col. 7, lines 18-21). It is disclosed that the concentration of the beclomethasone in the liquid medium can vary from about 0.1 to 60%, and preferably from 5-30% (w/w) (see col. 6, lines 19-22). Weidmann discloses that the surface modifiers can be present in the formulation in an amount from 0.1-90% or preferably from 20-60% based on the total weight of the dry particles (see col. 6, lines 23-28 and col. 10, lines 40-55). Wiedmann discloses filteration, but lacks teachings on sterile filtration.

Desai et al teach formulations for in vivo delivery of pharmacological agents in which the pharmacologically active agent is delivered in the form of suspended particles. There is also provided, a process of preparing unusually small **nanoparticles** of less than 200 nm in diameter, which can be **sterile-filtered**, through a 0.22 micron filter (see [0051]). Desai et al disclose methods for the preparation of substantially water insoluble pharmacologically active agents for in vivo delivery, said method comprising, combining an organic solvent having said active agent dissolved therein, water, a surfactant and a co-surfactant that spontaneously form a micro-emulsion and removing said organic solvent to yield a suspension of nanoparticles of said active agent in said

water (see [0093] to [[0100]). It is further disclosed that insoluble active agents include inhalant corticosteroids such as beclomethasone dipropionate and budesonide (see [0122] and [0146]).

Examples 4, 5 and 8 disclose a nanoparticle formation wherein the dispersion is sterile filtered.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have implemented the sterile filtration method as taught by Desai et al in the formulations and process of Wiedmann, since Wiedmann teaches filtration of nanoparticles of beclomethasone and tyloxapol. In other words, one of ordinary skill in the art would have been motivated to implement sterile filtration of Desai et al instead of simple filtration of Wiedmann because sterilized formulations are safer and beneficial to recipients. In other words, the claims would have been obvious because the technique for improving a particular product was part of the ordinary skill in the art, in view of the teaching of the technique for improvement in other situations. Specifically, it is shown that sterile filtration of solid dispersions of nanoparticles in liquid mediums is known in the art (as taught by Desai et al). Weidmann teaches the formulations.

Claims 1-7, 9-11 and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wood et al (WO 9625918) in view of Desai et al (US 20070117862).

Wood et al teach aerosols containing droplets of an aqueous **dispersion** of nanoparticles of insoluble **beclomethasone** particles having a surface modifier on the surface thereof. Representative examples of surface modifiers include gelatin, benzalkonium chloride, PVA, sorbitans, etc (see pages 6-7). A suitable surfactant is **tyloxapol** (see page 8), the particles are preferably less than 400 nm in size, or more preferably less than 250 and most preferably **less than 100 nm** in size (see page 16). The process of making such nanoparticles includes attrition and **filtration.** It is disclosed that the concentration of the beclomethasone in the liquid medium can vary from about 0.1 to 60%, and preferably from 5-30% (w/w) (see examples). Wood et al discloses that the surface modifiers can be present in the formulation in an amount from 0.1-90% or preferably from 20-60% based on the total weight of the dry particles. Wood et al discloses filteration, but lacks teachings on sterile filtration.

Desai et al, discussed above, teaches sterile filteration of dispersions of nanoparticles.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have implemented the sterile filtration method as taught by Desai et al in the formulations and process of Wood et al, since Wood et al teach filtration of nanoparticles of beclomethasone and tyloxapol. In other words, one of ordinary skill in the art would have been motivated to implement sterile filtration of Desai et al instead of simple filtration of Wood because sterilized formulations are safer and beneficial to

recipients. In other words, the claims would have been obvious because the technique for improving a particular product was part of the ordinary skill in the art, in view of the teaching of the technique for improvement in other situations. Specifically, it is shown that sterile filtration of solid dispersions of nanoparticles in liquid mediums is known in the art (as taught by Desai et al). Wood et al teaches the formulations.

Response to Arguments

Applicant's arguments filed 11/30/07 have been fully considered but they are not persuasive.

Applicant argues that “Desai does not teach or fairly suggest that its sterile filtration techniques can be applied to a non-polymeric nanoparticle” and also that “Desai differentiates its polymeric nanoparticles from what Desai considers to be "conventional" surface-stabilized nanoparticles, which are taught by Wiedmann”. Applicant continues that “Desai admits that he was unsuccessful in formulating nanoparticles of the active agent without using the polymeric core, e.g., by using "conventional surfactants” to stabilize the nanoparticles of the active agent”.

This is not persuasive because Desai et al teach that nanoparticles of active agents with surfactant and co-surfactants can be produced (see [0094] to [0100]). Suitable surfactants include nonionic surfactants such as Tween, Span, Triton, Pluronic, etc, and anionic, cationic and zwitterionic surfactants (see [0271] and [0295]).

Applicant also states that according to Desai’s disclosure, *it is not possible* to form nanoparticles while using conventional surfactants. Applicant refers to Examples 2

and 3 of Desai to show this point. This is not persuasive because Desai teach that "use of conventional surfactants ***alone*** results in formation of large crystals". Desai states that "it is not possible to form nanoparticles while using conventional surfactants **without** a polymeric core material". Firstly, the particles of instant claims require or allow for a second surfactant which can be a polymer (see instant claim 9). Thus the scope of instant claims is within the scope of Desai's disclosure. Secondly, even if Desai's disclosure was different from the instant claims, the formulations are taught by Weidmann and Wood et al, Desai was brought in and relied upon for the teachings of sterile filteration of dispersions of nanoparticles. It is disclosed and known in the art that sterile filters have a pore size of 0.2 micron. In order for any dispersions to go through the said filters, the particle size has to be at or less than 0.2 microns.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 571-272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mina Haghighatian/

Mina Haghighatian
Patent Examiner
February 18, 2008